REMARKS

Applicants thank Examiner Sheinberg for her time and courtesy she extended to Applicants' Representative during the personal interview on October 3, 2001, wherein the Examiner's Action mailed June 5, 2001, was discussed. As agreed, the following comments are submitted in response to the outstanding matters.

Extension of Time

A Petition has been filed under the provisions of 37 CFR §1.136 for an extension of time to respond to the Examiner's Action of June 5, 2001. The appropriate fee set forth in 37 CFR § 1.17 is filed herewith.

Claim Rejections - 35 USC § 112 first and second paragraphs

In order to advance the prosecution, claims 1 and 18-20 have been amended to more particularly point out the invention and to conform with U.S. Patent practice. Claims 1-20 are pending in the application.

Claim Rejections - 35 USC § 103

The Examiner rejected claims 1, 9-12, 14-16 and 18-20 under 35 U.S.C. § 103(a) as being unpatentable over Jain et al. (J.

Med. Chem, 1994). Additionally, the Examiner rejected claims 1, 4, 5, 7-16 and 18-20 under 35 U.S.C. § 103(a) as being unpatentable over Jain et al. (J. Med. Chem, 1994); and further in view of Lavender et al. (IEEE Comp. Graphics & App., 1992) and Chen et al. (Bio. org & Med. Chem. Letters, 1998).

It is respectfully submitted that the present claimed invention is patentable over the art of record for the following reasons. Accordingly, reconsideration of the Examiner's rejection is requested.

The characteristic features of the present invention can be understood by comparing it with the prior art described in page 1, line 27 to page 8, line 17. Here, Jain et al cited in the Office Action can be said to belong to "CoMFA" in the means that a common skeleton is necessary as a common portion in the molecules to be compared and the common skeleton is the dominant part of the molecules.

"In the field of development of medicines, the cooperative molecular field analysis (CoMFA) method is conventionally known as a method for predicting the activity characteristics of ligand molecules (see, e.g., R.D. III Cramer, et al., J. Am. Chem. So., 1988, 100, 5959).

In the CoMFA method, a CoMFA field is produced to five the three-dimensional expression of a chemical structure of ligand

molecule. The CoMFA field is derived by forming, e.g., a rectangular parallelepiped-shaped region surrounding a molecule, the activity characteristic of which is to be predicted considering lattice points, which are distributed in the surrounding region in the form of a lattice, as probe points, and putting probe atoms at the respective probe points to calculate energy of the interaction between the probe atoms and the components of the molecule, such as substituents.

In the CoMFA method, it is assumed that a portion occupying a major part of a molecule, the reaction characteristic of which is to be predicted, is a common skeleton serving as a common portion, and the substituted portions of molecules having a common skeleton are substituted by various substituents. On the basis of the correlation characteristics of the obtained CoMFA, the presence of similarity between the activity characteristics of the molecules having the common skeleton is determined.

However, in the CoMFA method, it is assumed that the molecules have the common skeleton, and when the prediction of the activity characteristic of a certain molecule is intended, the presence of similarity between activity characteristics is determined only between the certain molecule and another molecule having a common skeleton with the certain molecule.

Thus, it is not possible to determine the presence of similarity between reaction characteristics of molecules, which have quite different sizes and which do not have any common skeleton.

In addition, in the CoMFA method, a molecule, the reaction characteristic of which is to be predicted, is not decomposed into minute sites to derive characteristic values for each site, and one CoMFA field is obtained as the whole molecule. Therefore, it is not known how each of the sites of the molecule contributes to the reaction, so that it is not possible to accurately predict and consider the reaction characteristic of the molecule.

Moreover, in the CoMFA method, the rectangular parallelepiped surrounding the overlapped ligand molecules is different in accordance with the size of a target ligand molecule group, so that there is a limit that the obtained characteristic value depends on the target ligand molecule group.

In addition, the CoMFA method is applied to the prediction of activity and the design of a medicine in the development of the medicine, so that the CoMFA method can not be applied to the prediction of reactivity and the design of synthesis in the field of synthetic chemistry. There is no reaction characteristic predicting method serving as a guide to the prediction of

reactivity and the design of synthesis in the field of synthetic chemistry and as a guide to the prediction of activity and the design of a medicine in the development of the medicine.

It is therefore an object of the present invention to eliminate the aforementioned problems and to provide a molecular reaction characteristic predicting method, which can be applied to a wide field of chemistry including the field of synthetic chemistry as well as the field of development of medicines and which can accurately predict the presence of similarity between reaction characteristics of various molecules without limitations on common skeleton, and a reaction characteristic predicting map and computer-readable storage medium.

As shown above, in the case of Jain et al. (CoMFA), it is needed that the skeleton is common between the two molecules to be compared. As shown in Fig. 1 in Jain et al, the two molecules to be compared are positioned so that the two skeletons are superimposed with each other in the rectangular coordinate space where lattice points are distributed as probe points.

The present invention is very different from the case of Jain et al (CoMFA).

In the case of the present invention, for example, there is no procedure to position for superimposing two molecules to be

compared and there is no need to set lattice points distributed as probe points in the rectangular coordinate space.

In the case of the present invention, it is possible to compare whether there is similarity between reaction characteristics of molecules having quite different sizes and having no any common skeleton.

Some of the important features in claim 1 exist in "component space". Each "component space" includes on atom composing the molecule.

"A frontier surrounding surface" is defined as a component surrounding surfaces of each of said component spaces appearing outside on said molecule surrounding surface.

Each of "component spaces" having "a frontier surrounding surface" can show a guideline for estimating a reaction characteristics of the molecule. Then, it becomes possible to refer each of the component spaces individually as a guideline for estimating a reaction characteristics of the molecule.

The Examiner cited "the use of neural network" and "the Voronoi diagram" and mentioned to these. However, the Examiner seems to cite these terms only based on the fact she can find out these in the citation having the same technical field as to the present invention.

For example, the neural network is used for grouping the characteristic data in the present invention, but the neural network is used for positioning two molecules to be interposed in the citation, and the neural network is used in much different way between the present invention and the citation.

As shown in claim 8, " the Voronoi diagram" is introduced as on embodiment of said predetermined space dividing procedure 2 in claim 1.

The Examiner's assertion that one of ordinary skill would be motivated to form Applicants' claimed invention is respectfully incorrect. As the Examiner well knows, obviousness cannot be established by combining pieces of prior art absent some teaching, suggestion, or incentive supporting the combination. – Lavendar et al.

Accordingly, in view of the foregoing amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw the rejection of the claims to allow these claims and to find this application to be in allowable condition.

If the Examiner believes that a further conference would be of value in expediting the prosecution of this application, the Examiner is invited to telephone the undersigned to arrange for such a conference.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,
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Atty. Docket: P63431US0

Version with markings to show changes made.

In the Abstract:

Please insert the Abstract of Disclosure, attached as a separate sheet, at the end of the specification.

In the Claims:

Please amend claims 1 and 18-20 as follows:

1. (Amended) A molecular reaction characteristic predicting method for predicting a reaction characteristic of a molecule, said method comprising the steps of:

setting a molecule surrounding surface surrounding the molecule so as to be reflected in a spatial dimension of [a] the molecule, and assuming that a space surrounded by said molecule surrounding surface is a molecule surrounding space;

dividing said molecule surrounding space into a plurality of component spaces, by which a reaction characteristic of said molecule is characterized, in accordance with a predetermined space dividing procedure, and assuming that contour surfaces surrounding said component spaces are component surrounding surfaces, said molecule surrounding space being divided so as

that each component space of the plurality of component spaces includes therein each one atom composing the molecule;

assuming that a portion of each of said component surrounding surfaces appearing outside on said molecule surrounding surface is a frontier surrounding surface of each of said component spaces;

providing probe points on said frontier surrounding surface of each of said component spaces at regular intervals;

deriving a rate of said molecule surrounding space occupied by each of said component spaces, as a space occupied rate of each of said component spaces;

deriving electrostatic energies between a unit charge set at each of said probe points and charges of all of atoms of said molecule, for each of said probe points on said frontier surrounding surface of each of said component spaces, and deriving the sum of said electrostatic energies on said frontier surrounding surface of a corresponding one of said component spaces, as an electrostatic factor of said corresponding one of said component spaces;

deriving van der Waals energies between a probe atom, which is set at each of said probe points and which has a predetermined steric characteristic, and all of said atoms of said molecule, for each of said probe points on said frontier surrounding

surface of each of said component spaces, and deriving the sum of said van der Waals energies on said frontier surrounding surface of said corresponding one of said component spaces, as a steric factor of said corresponding one of said component spaces; and

assuming that said space occupied rate, said electrostatic factor and said steric factor are reaction characteristic values of said corresponding one of said component spaces, and predicting a reaction characteristic of said molecule on the basis of said reaction characteristic values of each of said component spaces.

18. (Amended) A molecular reaction characteristic predicting method comprising the steps of:

describing atomic spherical surfaces, each of which surrounds a corresponding one of atoms of a molecule;

assuming that a portion of each of said atomic spherical surfaces intersecting the atomic spherical surfaces of other atoms of said molecule is an interior spherical surface;

assuming that a portion of each of said atomic spherical surfaces other than said interior spherical surface is a frontier spherical surface, the frontier spherical surface being appeared outside;

providing probe points on each of said atomic spherical surfaces at regular intervals;

deriving a rate of occupied space as a space occupied rate of a corresponding one of said atoms, for each of said atoms;

deriving electrostatic energies between a unit charge set at each of said probe points and charges of all of said atoms of said molecule, for each of said probe points on said frontier spherical surface of each of said atoms;

deriving the sum of said electrostatic energies on said frontier surrounding surface of a corresponding one of said atoms, as an electrostatic factor of said corresponding one of said atoms;

deriving van der Waals energies between a probe atom, which is set at each of said probe points and which has a predetermined steric characteristic, and all of said atoms of said molecule, for each of said probe points on said frontier surrounding surface of each of said atoms;

deriving the sum of said van der Waals energies on said frontier surrounding surface of said corresponding one of said atoms, as a steric factor of said corresponding one of said atoms;

assuming that said space occupied rate, said electrostatic factor and said steric factor are reaction characteristic values of said corresponding one of said atoms; and

predicting a reaction characteristic of said molecule on the basis of said reaction characteristic values of each of said atoms.

19. (Amended) A reaction characteristic predicting map for predicting a reaction characteristic of a molecule, wherein referring to a molecular reaction characteristic predicting method for predicting a reaction characteristic of a molecule, said method comprising the steps of:

setting a molecule surrounding surface so as to be reflected in a spatial dimension of a molecule, and assuming that a space surrounded by said molecule surrounding surface is a molecule surrounding space;

dividing said molecule surrounding space into a plurality of component spaces, by which a reaction characteristic of said molecule is characterized, in accordance with a predetermined space dividing procedure, and assuming that contour surfaces surrounding said component spaces are component surrounding surfaces, said molecule surrounding space being divided so as

that each component space of the plurality of component spaces includes therein each one atom composing the molecule;

assuming that a portion of each of said component surrounding surfaces appearing outside on said molecule surrounding surface is a frontier surrounding surface of each of said component spaces;

providing probe points on said frontier surrounding surface of each of said component spaces at regular intervals;

deriving a rate of said molecule surrounding space occupied by each of said component spaces, as a space occupied rate of each of said component spaces;

deriving electrostatic energies between a unit charge set at each of said probe points and charges of all of atoms of said molecule, for each of said probe points on said frontier surrounding surface of each of said component spaces, and deriving the sum of said electrostatic energies on said frontier surrounding surface of a corresponding one of said component spaces, as an electrostatic factor of said corresponding one of said component spaces;

deriving van der Waals energies between a probe atom, which is set at each of said probe points and which has a predetermined steric characteristic, and all of said atoms of said molecule, for each of said probe points on said frontier surrounding

surface of each of said component spaces, and deriving the sum of said van der Waals energies on said frontier surrounding surface of said corresponding one of said component spaces, as a steric factor of said corresponding one of said component spaces; and

assuming that said space occupied rate, said electrostatic factor and said steric factor are reaction characteristic values of said corresponding one of said component spaces, and predicting a reaction characteristic of said molecule on the basis of said reaction characteristic values of each of said component spaces;

said space occupied rate, said electrostatic factor and said steric factor are derived for each of said component spaces forming said molecular surrounding space of each of a plurality of molecules, the reaction characteristics of which are to be predicted,

a plurality of sets of input data are generated so as to correspond to said plurality of component spaces of each of said plurality of molecules, each set of said plurality of sets of input data being formed by said space occupied rate, said electrostatic factor and said steric factor,

said plurality of sets of generated input data are processed in accordance with a technique of a self-organizing neural network, and

the processed result is displayed so as to indicate reaction characteristics of said plurality of molecules.

20. (Amended) A computer-readable storage medium having stored a program for predicting a reaction characteristic of a molecule, said program carrying out a process comprising the steps of:

setting a molecule surrounding surface surrounding the molecule so as to be reflected in a spatial dimension of a molecule, and assuming that a space surrounded by said molecule surrounding surface is a molecule surrounding space;

dividing said molecule surrounding space into a plurality of component spaces, by which a reaction characteristic of said molecule is characterized, in accordance with a predetermined space dividing procedure, and assuming that contour surfaces surrounding said component spaces are component surrounding surfaces, said molecule surrounding space being divided so as that each component space of the plurality of component spaces includes therein each one atom composing the molecule;

assuming that a portion of each of said component surrounding surfaces appearing outside on said molecule surrounding surface is a frontier surrounding surface of each of said component spaces;

providing probe points on said frontier surrounding surface of each of said component spaces at regular intervals;

deriving a rate of said molecule surrounding space occupied by each of said component spaces, as a space occupied rate of each of said component spaces;

deriving electrostatic energies between a unit charge set at each of said probe points and charges of all of atoms of said molecule, for each of said probe points on said frontier surrounding surface of each of said component spaces, and deriving the sum of said electrostatic energies on said frontier surrounding surface of a corresponding one of said component spaces, as an electrostatic factor of said corresponding one of said component spaces;

deriving van der Waals energies between a probe atom, which is set at each of said probe points and which has a predetermined steric characteristic, and all of said atoms of said molecule, for each of said probe points on said frontier surrounding surface of each of said component spaces, and deriving the sum of said van der Waals energies on said frontier surrounding surface of said corresponding one of said component spaces as a steric factor of said corresponding one of said component spaces; and

assuming that said space occupied rate, said electrostatic factor and said steric factor are reaction characteristic values

of said corresponding one of said component spaces, and predicting a reaction characteristic of said molecule on the basis of said reaction characteristic values of each of said component spaces.